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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,694	10/08/2004	Kenji Mori	MUR-043-USA-PCT	4087
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TOWNSEND & BANTA c/o PORTFOLIO IP PO BOX 52050 MINNEAPOLIS, MN 55402			EXAMINER HOLLOWAY, IAN KNOBEL	
			ART UNIT 4148	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/510,694	Applicant(s) MORI ET AL.	
	Examiner Ian K. Holloway	Art Unit 4148	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/8/2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☒ Claim(s) 10 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 October 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>(08/27/2007), (07/05/2005)</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

2. The drawings are objected to under 37 CFR 1.83(a) because they fail to show “**A formulation 1240 comprising the multipoint...**” as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 10 is objected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **A membrane is referenced, but said membrane was not mentioned in claim 1, but rather is found in claims 8 and 9.**

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 12 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim positively recites a part of the human body, **the skin and mucosa**, and is non-statutory matter. The device must be **“... adapted to be applied ...”**

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1, 2, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Crawford et al. (US Patent 6662044)** in view of **Howey (NPL, *Diabetes* Vol. 43)**.

Regarding **Claims 1 and 2**, **Crawford et al.** discloses the use of two different electric field applying means, iontophoresis and electroporation, (Column 1, lines 22-24) to distribute therapeutic agents (Column 4, lines 23-24).

Crawford et al. fails to disclose the use of insulin lispro.

However, **Howey** teaches the similarities between lispro and human insulin. Lispro simply has the positions 28 and 29 in the β -chain switched. The study, conducted by IUPUI, was able to conclude, "strongly support our contention that LYSPRO and human insulin are equipotent" (page 400, column 1, lines 1-3).

Crawford et al. discloses the claimed invention except for the use of insulin lispro. **Howey** teaches that it is known to use insulin lispro in place of insulin. It would have been obvious to one of ordinary skill in the art at the time of the invention was made to utilize insulin lispro as taught by **Howey**, since **Howey** states at column 1, lines 1-3 that such modification would be an equivalent substance.

Since the marketplace reflects the reality that applying insulin lispro as a therapeutic agent is commonplace, it would have been obvious to one of ordinary skill in the art of electroporation and iontophoresis as shown in **Crawford et al.** with the use of insulin lispro as shown in **Howey**, in order to gain the commonly understood benefits of such adaptation, such as using insulin lispro in a iontophoresis electrode.

Regarding **Claim 12**, the device of **Crawford et al.** as modified by **Howey** discloses the use of applying a patch to skin. (Column 3, line 40, **Crawford et al.**)

9. Claims 3, 4, 15-17, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Crawford et al.** in view of **Howey** in further view of **Mori et al.** (US **PgPub 2001/0039393**)

Regarding **Claim 3**, the device of **Crawford et al.** as modified by **Howey** discloses the invention claimed as stated above except for the range of current used by the electrodes.

However, **Mori et al.** teaches a similar electroporation device where the current range used is .01 to 10 mA (Claim 40).

The device of **Crawford et al.** as modified by **Howey** discloses the claimed invention except for the optimum current range. It would have been obvious to one of ordinary skill in the art at the time the invention was made to test within all reasonable ranges, including those set forth by **Mori et al.**, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Regarding **Claim 4**, the device of **Crawford et al.** as modified by **Howey** fails to disclose the range of voltage used by the electrodes.

However, **Mori et al.** teaches a similar electroporation device where the Voltage range used is .1 to 50 V (Claim 42)

The device of **Crawford et al.** as modified by **Howey** discloses the claimed invention except for the optimum voltage range. It would have been obvious to one of ordinary skill in the art at the time the invention was made to test within all reasonable ranges, including those set forth by **Mori et al.**, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Regarding **Claim 15**, the device of **Crawford et al.** modified by **Howey** discloses the use of combination electroporation (315, **Crawford**) and iontophoresis (302, **Crawford**) electrodes that are disposed on a membrane. The system also utilizes a drug reservoir and insulin lispro.

The device of **Crawford et al.** as modified by **Howey** fails to disclose the overall design of the electrode.

However, **Mori et al.** teaches the overall design of the electrode, including having a backing; an iontophoresis electrode disposed on the backing; and the presence of a membrane (Fig. 3).

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to rearrange the parts of **Crawford et al.** as taught by **Mori et al.**, since such modification would result in a easier to build electrode.

Because both **Crawford et al.** and **Mori et al.** teach electrodes for use with iontophoresis and electroporation, it would have been obvious to one skilled in the art to substitute one electrode geometry for the other to achieve the predictable result of a usable electrode.

Regarding **Claims 16 and 17**, the device of **Crawford et al.** as modified by **Howey** discloses the invention as claimed above except for the presence and porosity of the membrane.

However, **Mori et al.** teaches the presence of a membrane. The membrane has a pore size of about 0.01 μm to 10 μm . (Page 5, Claim 2)

The device of **Crawford et al.** as modified by **Howey** discloses the claimed invention except for the presence of the membrane. **Mori et al.** teaches that it is known to use a membrane with electrodes. It would have been obvious to one of ordinary skill in the art at the time of the invention was made to use a membrane as taught by **Mori et al.**, since such modification would make the device more effective, since it would be agent permeable (Paragraph 19, **Mori**).

Since the marketplace reflects the reality that applying membranes to electrodes is commonplace, it would have been obvious to one of ordinary skill in the art of electroporation and iontophoresis as shown in **Crawford et al.** as modified by **Howey** with the use of a membrane as shown in **Mori et al.**, in order to gain the commonly understood benefits of such adaptation, such as a more effective electrode.

In addition, **Crawford et al.** as modified by **Howey** discloses the claimed invention except for the optimum porosity of the membrane.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to test within all reasonable ranges, including those set forth by **Mori et al.**, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or working ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Regarding **Claim 20**, the device of **Crawford et al.** as modified by **Howey** and **Mori et al.** discloses that the number of electrodes utilized in **Crawford et al.**'s disclosure is not limited; therefore, more than one contact point could be used.

10. Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Crawford et al.** in view of **Howey** in further view of **Jacobsen et al. (US patent 4416274)**

Regarding **Claims 5** and **6**, the device of **Crawford et al.** as modified by **Howey** discloses the invention as claimed above except for the use of a hydrophilic matrix.

However, **Jacobsen** teaches the use of a hydrophilic matrix used in iontophoresis. The matrix can be constructed from many different materials, including polyvinyl alcohol. (Column 3, lines 33-37)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to choose to make the matrix out of hydrophilic material, Since it has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. In re Leshin, 125 USPQ 416.

11. Claims 7-10 and 18 rejected under 35 U.S.C. 103(a) as being unpatentable over **Crawford et al.** in view of **Howey** in further view of **Mori et al.**

Regarding **Claims 7** and **9**, the device of **Crawford et al.** as modified by **Howey** discloses the invention as claimed above except for the use of a membrane.

However, **Mori et al.** teaches the presence of a membrane. The membrane has a pore size of about 0.01 μm to 10 μm . (Page 5, Claim 2)

The device of **Crawford et al.** as modified by **Howey** discloses the claimed invention except for the presence of the membrane. **Mori et al.** teaches that it is known to use a membrane with electrodes. It would have been obvious to one of ordinary skill in the art at the time of the invention was made to use a membrane as taught by **Mori et al.**, since such modification would make the device more effective.

Since the marketplace reflects the reality that applying membranes to electrodes is commonplace, it would have been obvious to one of ordinary skill in the art of electroporation and iontophoresis as shown in **Crawford et al.** as modified by **Howey** with the use of a membrane as shown in **Mori et al.**, in order to gain the commonly understood benefits of such adaptation, such as a more effective electrode.

Regarding **Claim 8**, the device of **Crawford et al.** discloses the presence of electroporation electrodes (Fig. 3, electrode gaps are formed for electroporation, **Crawford**) on a membrane. (Column 9, lines 62-67, **Crawford**)

Regarding **Claim 10**, the device of **Crawford et al.** as modified by **Howey** and **Mori et al.** discloses the invention claimed above except for the membrane's ability to retain insulin lispro.

However, one of ordinary skill in the art at the time of the invention would know to allow the membrane to retain whatever material it is supposed to have permeability to.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make it so the membrane was not impermeable to the material it is supposed to carry since it was known in the art that any material that allows a substance to pass through it, must also be able to retain it for some amount time.

Regarding **Claim 18, Crawford et al.** discloses the use of combination electroporation (315) and iontophoresis (302) electrodes that are disposed on a membrane (Column 1, lines 22-24).

Crawford et al. fails to disclose many other aspects of the invention.

However, **Howey** teaches the use of insulin lispro (page 400, column1, lines 1-3).

The device of **Crawford et al.** as modified by **Howey** fails to disclose many other components.

However, **Mori et al.** teaches a backing, an iontophoresis electrode disposed on the backing, a hydrophilic matrix base disposed on the iontophoresis electrode, a liner disposed on the hydrophilic matrix base, a retaining membrane which is disposed on the liner (Fig. 3).

12. Claims 11 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Howey** in view of **Crawford et al.** in further view of **Mori et al.** in further view of **Murdock (US PgPub 2002/0058903)**.

Regarding **Claims 11 and 19**, the device of **Crawford et al.** as modified by **Howey** and **Mori et al** discloses the invention claimed above except for the storage of lispro in the dry state.

However, **Murdock** teaches the use of anhydrous, dry, drug reservoirs used in iontophoresis. (Abstract)

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to include an anhydrous drug reservoir as taught by **Murdock**, since such modification would make the electrode longer lasting. Thus, it would have been obvious to one of ordinary skill in the art to apply anhydrous reservoirs as taught in **Murdock**, to improve the electrode of **Crawford et al.** for the predictable result of creating an electrode with a longer shelf life (Paragraph 21, **Murdock**).

13. Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Crawford et al.** in view of **Howey** in further view of **Miller et al. (US Patent 7137975)**

Regarding **Claims 13**, the device of **Crawford et al.** as modified by **Howey** discloses an electroporation-iontophoresis (**Crawford**) formulation containing insulin lispro (page 400, column1, lines 1-3, **Howey**).

The device of **Crawford et al.** as modified by **Howey** fails to disclose the counter electrode and the power supply.

However, **Miller et al.** teaches the use of an electrode and a counter electrode (202, 204) and a power supply (206) (Figure 9). It further teaches two attachment points on the power supply (206, figure 9)

The device of **Crawford et al.** as modified by **Howey** discloses the claimed invention except for the counter electrodes and their attachment points on a power supply. **Miller et al.** teaches that it is known to use multiple electrodes and a power supply for iontophoresis. It would have been obvious to one of ordinary skill in the art at the time of the invention was made to include the power supply as part of the system as taught by **Miller et al.**, since such modification would make the device usable. Thus, it would have been obvious to one having ordinary skill in the art to include the power supply taught by **Miller et al.** in view of the electrodes shown by **Crawford et al.**, since the electrode design is in no way dependent on which power supply is utilized. The electrodes could be used in combination with **Miller et al.**'s power supply to achieve the predictable result of performing electrophoresis and iontophoresis.

Regarding **Claim 14**, the device of **Crawford et al.** as modified by **Howey** fails to disclose a connecting port used for iontophoresis and a connecting port used for electroporation.

However, **Miller et al.** discloses a connecting port used for iontophoresis and a connecting port used for electroporation (206, Fig. 9).

it would have been obvious to one having ordinary skill in the art to include a connecting port used for iontophoresis and a connecting port used for electroporation taught by **Miller et al.** in view of the electrodes shown by **Crawford et al.**, since the combination with **Miller et al.**'s connecting ports will achieve the predictable result of performing electrophoresis and iontophoresis.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian K. Holloway whose telephone number is 571-270-3862. The examiner can normally be reached on 8-5, Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terrell L. McKinnon can be reached on 571-272-4797. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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1-3-08
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